REMARKS

Claims 1-43 are pending. Claims 9-15 and 20-42 are under examination.

Rejection Under 35 U.S.C. § 101 and § 112, First Pargraph

The rejections of claims 9-15 and 20-42 under 35 U.S.C. § 101 and under § 112, first paragraph, as allegedly lacking utility are respectfully traversed. Applicant respectfully maintains, for the reasons of record, that the claimed nucleic acids have a specific, substantial and credible utility.

As discussed in the previous response, the primary principle of the Utility Examination Guidelines published on January 5, 2001, *66 Fed. Reg. 1092* (January 5, 2001), is the requirement that the utility asserted be well-established or specific, substantial and credible, as judged by one of ordinary skill in the art. The Examiner nevertheless is reminded that the Guidelines and the legal analysis govern the internal operations of the USPTO, but do not have the force and effect of law and cannot, therefore, constitute substantive rules creating or altering the rights or obligations of any party. *66 Fed. Reg. 1097* (January 5, 2001).

Applicant respectfully maintains that the specification teaches a specific, substantial and credible utility. Analysis of the Nope sequence revealed that the protein encoded by the Nope nucleic acid sequence contains four immunoglobulin domains and five fibronectin-type domains, has structural similarity to DCC, Punc and NCAM, and most closely resembles cell adhesion molecules (page 46, lines 8-17). The specification further teaches the function of these structurally related proteins as axonal guidance receptors (page 49, line 22, to page 50, line 7). The specification also teaches the developmental expression of Nope, including its expression in cells of the nervous system (Example II, pages 46-48, in particular page 47, line 27, to page 48, line 16). The specification clearly provides an explicit teaching of a specific, substantial and credible utility of the Nope polynucleotide in that it encodes a protein expressed in the nervous system and that functions as an axonal guidance receptor.

Applicants respectfully disagree with the assertion in the Office Action on page 3, first paragraph, that the expression of Nope polynucleotides in the ventricular zone in the brain, hippocampus, the pririform cortex, thalamic nuclei and foliae of the cerebellum does not mean

that the polynucleotide is an appropriate target to regulate the development of the nervous system and related biological functions, as taught in the specification. The Office Action asserts that brain, hippocampus, the piriform cortex, thalamic nucleic and foliae of the cerebellum can express many polypeptides, such as constitutively expressed polypeptides, which are not appropriate targets. However, the fact that these nerve tissues can express proteins that are not appropriate targets is irrelevant to Nope being an appropriate target. The specification teaches that Nope is expressed in the developing mouse embryo in the notochord, in developing muscle tissues and in the developing nervous system (page 47, line 10, to page 48, line 16). Nope expression is concentrated in the ventricular zone in the brain and in the hippocampus, the piriform cortex, thalamic nucleic and foliae of the cerebellum of adult brain (page 48, lines 3-16). The specification teaches that Nope functions in cells of the nervous system that arise late in gestation (page 48, lines 8-11). Applicant maintains that the specification provides a clear and credible teaching of a functional role of Nope in neuronal development.

Applicants appreciate the Examiner pointing out that the Nope gene has sequence homology to STS markers that map to human chromosome 15 and the opportunity to clarify the record. Applicants apologize for any confusion and wish to clarify that the specification teaches that the Nope gene shows sequence homology to two human STS markers that map to a locus on chromosome 15 that is linked to Bardet-Biedl syndrome 4 (page 57, lines 4-9). The mouse Nope gene maps to mouse chromosome 9 (page 53, line 10, to page 55, line 10). The genes for Nope, Punc and Neogenin are located on mouse chromosome 9 (page 55, lines 1-4). Neogenin maps to a region of mouse chromosome 9 that is syntenic to the region on human chromosome 15 where Neogenin has been placed on the cytogenetic map (page 55, lines 11-17). The mapping of Nope to a gene cluster of mouse chromosome 9 that is syntenic with a gene cluster of human chromosome 15 and the homology of Nope to human STS markers on human chromosome 15 corroborates Applicant's assertion of the utility of the claimed Nope polynucleotide.

Applicant refers to the MPEP, § 2107.01, as it relates to utility rejections. In particular under the section "Specific Utility" (MPEP page 2100-32), an example of a claim to a polynucleotide that does not satisfy the utility requirement is a polynucleotide with a disclosed use as a "gene probe" or "chromosome marker" "in the absence of a disclosure of a specific DNA target" (emphasis added). In contrast to this example in the MPEP, the claimed Nope

encoding nucleic acids map to a specific chromosome location on mouse chromosome 9 that includes a gene cluster syntenic to chromosome 15, and the specification therefore clearly teaches a specific DNA target.

With regard to the claimed Nope encoding nucleic acids, the specification teaches that the nucleic acid encodes a polypeptide having four immunoglobulin domains and five fibronectin-type domains, both of which are well characterized structural domains (page 46, lines 8-17). In addition, the specification teaches that Nope is related to axonal guidance receptors (page 49, line 22, to page 50, line 3). Furthermore, the specification teaches that Nope is expressed in the nervous system, consistent with its role in axonal guidance. Therefore, the claimed nucleic acids encoding Nope are correlated in the specification with well known structural motifs, proteins with known function, and tissue expression consistent with that function.

As discussed above, Applicant respectfully submits that the immunoglobulin and fibronectin domains are well known structural motifs. While it is known that proteins with different sequences can fold similarly and have similar functions and can have similar functions with different structures, as asserted in the Office Action, Applicant is unaware of the basis for the assertion in the Office Action on page 4 that proteins with very similar sequence fold up differently and respectfully request that the Examiner provide evidence that proteins with very similar sequences fold differently. Even so, the immunoglobulin and fibronectin domains are well characterized structural domains present on cell surface receptors and diffusible ligands that function as binding domains (page 12, line 7, to page 14, line 29). A subgroup of the immunoglobulin superfamily has been associated with migration and guidance of axonal growth cones (page 13, line 1, to page 14, line 29). Therefore, Applicants respectfully disagree with the assertion in the Office Action on page 4 that functional relatedness is not credible in the face of evidence in the art that structurally related polypeptides are frequently dissimilar functionally. To the contrary, Applicant respectfully submits that the teachings of the specification support a function and credible utility.

With respect to the reference by Marg et al., J. Cell Biol. 145:865-876 (1999), Applicant respectfully submits that this reference corroborates Applicants assertion that immunoglobulin domains are conserved and function in binding. The Office Action asserts that Marg et al.

describes a long and short form of neurotractin that share 100% identity but different functions. However, Marg et al. in fact discloses that the short and long form of neurotractin do share similar functions in that they bind to CEPU-1 and LAMP. The fact that they may have different affinities for CEPU-1 and LAMP does not change the shared function of binding to the short and long form of neurotractin to the same ligands. Thus, it is respectfully submitted that Marg et al. corroborates Applicant's position that the immunoglobulin domains are well characterized binding domains that one skilled in the art would understand to have a predictable function in binding, even if the specific binding partner is not known.

Moreover, referring to the utility guidelines referenced above, the issue of using sequence homology is addressed under Comment 19. In particular, the guidelines indicate that "when a patent application claiming a nucleic acid asserts a specific, substantial, and credible utility, and bases the assertion upon homology to existing nucleic acids or proteins having an accepted utility, the asserted utility must be accepted by the examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such an assertion. "[A] 'rigorous correlation" need not be shown in order to establish a practical utility: 'reasonable correlation is sufficient," referencing *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1565, 39 USPQ2d 1896, 1900 (Fed. Cir. 1996). The guidelines further indicate that "[W]hen a class of proteins is defined such that the members share a specific, substantial and credible utility, the reasonable assignment of a new protein to the class of sufficiently conserved proteins would impute the same specific, substantial and credible utility to the assigned protein."

Applicant respectfully maintains that, at least for the reasons described above, the claimed nucleic acids have a specific, substantial and credible utility. Furthermore, the utility guidelines indicate that "Office personnel are reminded that they must treat as true a statement of fact made by an applicant in relation to an asserted utility, unless countervailing evidence can be provided that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement." Applicant respectfully submits that, based on the teachings in the specification and what was well known to those skilled in the art, one of ordinary skill in the art would have understood that the claimed Nope encoding nucleic acid molecules have a specific, substantial and credible utility. Accordingly, Applicant respectfully requests that the utility rejection under 35 U.S.C. § 101 and 112 be withdrawn.

Rejection Under 35 U.S.C. § 112, First Paragraph

The rejection of claims 9, 10 and 14 under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description is respectfully traversed. Applicant maintains, for the reasons of record, that the specification provides sufficient description and guidance for the claimed nucleic acids.

As discussed previously, the specification teaches that a modification of a nucleic acid can include one or several nucleotide additions, deletions or substitutions with respect to a reference sequence, including a substantially the same nucleotide sequence that can hybridize under moderately stringent or higher stringency conditions (page 9, lines 16-30). The specification also teaches various stringency conditions (page 24, line 15, to page 25, line 18). Therefore, Applicant respectfully maintains that the specification provides sufficient description and guidance for the claimed nucleic acid molecules and modifications thereof. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

In light of the amendments and remarks herein, Applicant submits that the claims are now in condition for allowance and respectfully requests a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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